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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,888	02/10/2004	Rainer Endermann	Le A 36 499	1423

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,888	ENDERMANN ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10,12 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,10,12 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 21, 2010 has been entered.

Claim Rejections 35 U.S.C. 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 2, 10, 12 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "betaine" in claim 1 is used by the claim to mean "zwitterionic compound" (as now applicants argued), while the accepted meaning is "A **betaine** in chemistry is any neutral chemical compound with a positively charged cationic functional group such as an quaternary ammonium or phosphonium cation (generally: onium ions) which *bears no hydrogen atom* and with a negatively charged functional group such as a carboxylate group which may not be adjacent to

the cationic site. A betaine thus may be a specific type of zwitterion. Historically the term was reserved for trimethylglycine only." The term is indefinite because the specification does not clearly redefine the term.

Claim Rejections 35 U.S.C. 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Because of the ambiguity of the claims (see the rejection above), the claims are interpretated broadly to encompass both the compound represented by formula (III) its betaine salts.

3. Claims 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Pikiewicz et al. (US 2004/0009126 A1).

4. Pikiewicz et al. teach a method of treating bacterial lung infection comprising locally administration of ciprofloxacin by inhalation, wherein the ciprofloxacin is in the form of particle and may be in the form of dry powder. See, particularly, the abstract, paragraphs [0064] and [0069], and the claims.

Claim Rejections 35 U.S.C. 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al.

Mayer et al. treated anthrax lung infection by administering to the patients ciprofloxacin. The administration is carried out intravenously. See, particularly, the abstract, pages 2550 and 2551. Mayer et al. further disclosed that it is well known that ciprofloxacin is effective against anthrax and is a standard treatment of anthrax. See, page 252, the right column.

Mayer et al. do not teach expressly local administration as herein claimed.

However, Li et al. teach ciprofloxacin administration intravenously or orally have relatively unfavorable pharmacokinetic profile in the lower respiratory track. Li also disclosed that Aerosol inhalation as means of drug delivery to the respiratory tract has been well established in the treatment of lung disease, and dry powder inhaler have received increasing attention in the art. Li et al. further teaches a ciprofloxacin loaded particles for dry powder inhaler delivery to the respiratory track by inhalation. See, particularly, the abstract and introduction at page 825.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use dry powder inhaler for delivery ciprofloxacin composition, such as those disclosed by Li, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection.

A person of ordinary skill in the art would have been motivated to use dry powder inhaler for delivery ciprofloxacin composition, such as those disclosed by Li, directly to respiratory

track for treatment of respiratory track bacterial infection, such as anthrax infection because the delivery method is more effective than intravenous or oral delivery. As to patient's conditions recited in claim 15, note, an antibiotics agent known to be useful against bacterial infection would have expected to effective against the bacterial infection in patients with other medical conditions. Therefore, one of ordinary skill in the art would have been motivated to treat the bacterial infection of patients with cystic fibrosis, chronic obstructive pulmonary disease or bronchiactasis.

7. Claims 1, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pikiewicz et al. (US 2004/0009126 A1) in view of Kanikanti et al. (WO 02/00219 A1, US 2004/0024018 A1 is a English equivalence).

8. Pikiewicz et al. teach a method of treating bacterial lung infection comprising locally administration of ciprofloxacin by inhalation, wherein the ciprofloxacin or its salt, is in the form of particle and may be in the form of dry powder. See, particularly, the abstract, paragraphs [0064] and [0069], and the claims.

9. Pikiewicz et al. do not teach expressly the employment of the particular salt, ciprofloxacin betaine.

10. However, Kanikanti et al. teaches that ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose. See, particularly, paragraphs [0039]-[0047].

11. Therefore, it would have been obvious to use ciprofloxacin betaine as a ciprofloxacin salt in Pikiewicz's method.

12. A person of ordinary skill in the art would have been motivated to use ciprofloxacin betaine as a ciprofloxacin salt in Pikiewicz's method because ciprofloxacin betaine is one of few known salt of ciprofloxacin. Furthermore, as stated in KSR vs. Teleflex, where the court states:

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. **If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.** In that instance the fact that a combination was obvious to try might show it was obvious under section 103." In the instant case, it would have been obvious to try the known salts of ciprofloxacin for an optimal therapeutical result. Since there are not many known ciprofloxacin salts. As to patient's conditions recited in claim 15, note, an antibiotics agent known to be useful against bacterial infection would have expected to effective against the bacterial infection in patients with other medical conditions. Therefore, one of ordinary skill in the art would have been motivated to treat the bacterial infection of patients with cystic fibrosis, chronic obstructive pulmonary disease or bronchiactasis.

13. Claims 1, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al. and Kanikanti et al. (WO 02/00219 A1, US 2004/0024018 A1 is a English equivalence).

Mayer et al. treated anthrax lung infection by administering to the patients ciprofloxacin. The administration is carried out intravenously. See, particularly, the abstract, pages 2550 and

2551. Mayer et al. further disclosed that it is well known that ciprofloxacin is effective against anthrax and is a standard treatment of anthrax. See, page 252, the right column.

Mayer et al. do not teach expressly local administration as herein claimed or the employment of ciprofloxacin betaine.

14. However, Li et al. teach ciprofloxacin administration intravenously or orally have relatively unfavorable pharmacokinetic profile in the lower respiratory track. Li also disclosed that Aerosol inhalation as means of drug delivery to the respiratory tract has been well established in the treatment of lung disease, and dry powder inhaler have received increasing attention in the art. Li et al. further teaches a ciprofloxacin loaded particles for dry powder inhaler delivery to the respiratory track by inhalation. See, particularly, the abstract and introduction at page 825. Kanikanti et al. teaches that ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose. See, particularly, paragraphs [0039]-[0047].

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use dry powder inhaler for delivery ciprofloxacin composition, such as ciprofloxacin betaine, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection.

A person of ordinary skill in the art would have been motivated to use dry powder inhaler for delivery ciprofloxacin composition, such as such as ciprofloxacin betaine, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection because the delivery method is more effective than intravenous or oral delivery, and ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose. As to

patient's conditions recited in claim 15, note, an antibiotics agent known to be useful against bacterial infection would have expected to effective against the bacterial infection in patients with other medical conditions. Therefore, one of ordinary skill in the art would have been motivated to treat the bacterial infection of patients with cystic fibrosis, chronic obstructive pulmonary disease or bronchiactasis.

Response to the Arguments

15. Applicants' amendments and remarks submitted June 21, 2010 have been fully considered, but are not persuasive with respect to the rejections set forth above.

16. Applicants' remarks about the definition of Betaine are not persuasive. Particularly, extrinsic reference does not support applicants' conclusion. The definition of "betaine" by IUPAC is:

Originally, the compound betaine, $(CH_3)_3N^+-CH_2C(=O)O^-$ *N,N,N*-trimethylammonioacetate, and similar zwitterionic compounds derived from other amino acids. By extension, neutral molecules having charge-separated forms with an onium atom ***which bears no hydrogen atoms*** and that is not adjacent to the anionic atom. Betaine cannot be represented without formal charges. (emphasis added).

Therefore, even with broadened definition, betaine does not read on the free form (inner salt) of ciprofloxacin and enrofloxacin. Further, nowhere in the specification ever define "betaine" beyond the art accepted definition. Thus, one of ordinary skill in the art, at the time the claimed invention was made, would not definitely construe the claims as what applicant argued. Indefinite presented in the claims as to the meanings of "betaine."

17. Applicants contend that the claims are not anticipated by Pilkeiwicz because the ciprofloxacin used by Pilkeiwicz is in a water-soluble salt form, vs. the non-salt form or slightly water soluble salt claimed. Applicants erred in reading the particular example as a limitation of the teaching. As it is well settled that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). It is noted that Pilkeiwicz claims the composition comprises an anti-infective agent in claim 1, without the requirement that the agent be a salt. Only dependent claim 15 and 16 further limit the agent to be a salt. See, the claims. Therefore, Pilkeiwicz clearly teaches the employment of non-salt form of anti-infective agent. For the salt form, Pilkeiwicz does not require the water solubility. Further, there is no evidence in Pilkerwicz reference shows that the so called CIPRO stock solution is a water solution of ciprofloxacin hydrochloride. Note ciprofloxacin is soluble in organic solvent.

For the rejections over Meyer et and Li et al., applicant again erred in reading the example in Li as the limitation of the teaching by Li. Li reference never teach or suggest that the ciprofloxacin has to be in salt form or be water soluble. Li teach the local delivery of ciprofloxacin in encapsulated dry particles form.

With respect to the rejections citing Kanikanti, applicants particularly argue that there is no motivation to combine the insoluble ciprofloxacin. The arguments are not persuasive. It is noted that definition of "insoluble" herein is insoluble in *water*. It would have been within the skill of ordinary artisan to make a dry powder of ciprofloxacin betaine. Note the primary reference (such as Pilkeiwicz and Li) does not require ciprofloxacin be water soluble.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1627